

产品名称: **Palbociclib isethionate**

产品别名: 帕博西尼羟乙基磺酸盐 ; **PD 0332991 isethionate**

生物活性:

Description	Palbociclib isethionate is a highly selective inhibitor of CDK4/6 with IC ₅₀ s of 11 nM/16 nM, respectively.				
IC₅₀ & Target	Cdk4/cyclin D3	Cdk4/cyclin D1	Cdk6/cyclin D2	DYRK1A	MAPK
	9 nM (IC ₅₀)	11 nM (IC ₅₀)	16 nM (IC ₅₀)	2000 nM (IC ₅₀)	8000 nM (IC ₅₀)
In Vitro	<p>Palbociclib exhibits absolute selectivity for CDK4/6 with little or no activity against other CDKs. Palbociclib is effective at reducing Rb phosphorylation at Ser⁷⁸⁰ and Ser⁷⁹⁵ in MDA-MB-435 breast carcinoma cells with IC₅₀ of 66 nM and 63 nM, respectively. Palbociclib is a potent inhibitor of cell growth and suppresses DNA replication by preventing cells from entering S phase. Palbociclib inhibits thymidine incorporation into the DNA of Rb-positive human breast (such as MDA-MB-435, MCF-7), colon (H1299), and lung carcinomas (Colo-205) as well as human leukemias (CRRF-CEM and K562), with IC₅₀ values ranging from 0.04-0.17 μM. Palbociclib significant increases the percentage of MDA-MB-453 in G1 period[1]. Palbociclib inhibits phosphorylation of Rb in cycling CD138+ primary bone marrow myeloma cells, nontransformed primary B cells, MM1.S and CAG HMCLs cells line with IC₅₀ of <0.1 μM, 0.05 μM, and 60-70 nM, respectively. Palbociclib treatment also induces G1 arrest of CD138+ primary bone marrow myeloma and nontransformed primary B cells. Palbociclib induces G1 arrest in MM1.S with IC₅₀ of appr 0.05 μM[2]. Palbociclib preferentially inhibits proliferation of luminal estrogen receptor-positive (including HER2-positive) human breast cancer cell lines. Palbociclib increases gene expression of pRb and cyclin D1 and decreases gene expression of CDKN2A (p16) in most sensitive lines. Palbociclib enhances sensitivity to tamoxifen in cell lines with conditioned resistance to ER blockade[3].</p>				
In Vivo	<p>Palbociclib(150 mg/kg. p.o.) produces rapid Colo-205 colon carcinoma xenografts regressions and a corresponding tumor growth delay. Palbociclib (150 mg/kg, p.o.) induces complete tumor stasis and cell kill in MDA-MB-435 breast carcinoma. Palbociclib (150 mg/kg) also induces significant tumor regression in mice bearing the SF-295 glioblastoma xenografts, and in ZR-75-1 breast and PC-3 prostate tumor models (complete suppression of tumor growth). Palbociclib (150 mg/kg) suppresses Rb Ser⁷⁸⁰ phosphorylation in MDA-MB-435 breast carcinoma over the full 24-hour period. Palbociclib (150 mg/kg) down-regulates expression of four E2F-regulated genes CDC2, CCNE2, TK1, and TOP2A in Colo-205 carcinoma xenografts[1]. Palbociclib also rapidly inhibits myeloma tumor growth[2].</p>				
Solvent&Solubility	<p><i>In Vitro:</i></p> <p>H₂O : ≥ 66.66 mg/mL (116.20 mM)</p> <p>* "≥" means soluble, but saturation unknown.</p>				
	<div>Preparing Stock Solutions</div>	<div>Solvent Mass Concentration</div>	1 mg	5 mg	10 mg
		1 mM	1.7432 mL	8.7160 mL	17.4319 mL
		5 mM	0.3486 mL	1.7432 mL	3.4864 mL
		10 mM	0.1743 mL	0.8716 mL	1.7432 mL
	<p>*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。</p> <p>储备液的保存方式和期限 -80℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用， -20℃ 储存时，请在 1 个月内使用。</p>				

References	<p>[1]. Fry DW, et al. Specific inhibition of cyclin-dependent kinase 4/6 by PD 0332991 and associated antitumor activity in human tumor xenografts. <u>Mol Cancer Ther</u>, 2004, 3(11), 1427-1438.</p> <p>[2]. Baughn LB, et al. A novel orally active small molecule potently induces G1 arrest in primary myeloma cells and prevents tumor growth by specific inhibition of cyclin-dependent kinase 4/6. <u>Cancer Res</u>. 2006 Aug 1;66(15):7661-7.</p> <p>[3]. Finn RS, et al. PD 0332991, a selective cyclin D kinase 4/6 inhibitor, preferentially inhibits proliferation of luminal estrogen receptor-positive human breast cancer cell lines in vitro. <u>Breast Cancer Res</u>. 2009;11(5):R77.</p>
实验参考:	
Cell Assay	Cells are seeded in duplicate at 5,000 to 10,000 cells per well in 24-well plates. The day after plating, different concentrations of Palbociclib are added. Control wells without drug are also seeded. At the end of incubation, cells are trypsinized and placed in Isotone solution and counted immediately using a Coulter Z2 particle counter. [3]
Animal Administration	Mice (18-22 g) are randomized and then implanted s.c. with tumor fragments (appr 30 mg) into the region of the right axilla. Treatment is initiated when tumors reach 100 to 150 mg. Palbociclib is given according to the schedule and dose indicated in the table and figure legends by gavage as a solution in sodium lactate buffer (50 mM, pH 4.0) based on mean group body weight. In all experiments, there are 12 mice in the control group and 8 mice each in the treated groups. Additional details for each experiment are given in the table legends. [1]
References	<p>[1]. Fry DW, et al. Specific inhibition of cyclin-dependent kinase 4/6 by PD 0332991 and associated antitumor activity in human tumor xenografts. <u>Mol Cancer Ther</u>, 2004, 3(11), 1427-1438.</p> <p>[2]. Baughn LB, et al. A novel orally active small molecule potently induces G1 arrest in primary myeloma cells and prevents tumor growth by specific inhibition of cyclin-dependent kinase 4/6. <u>Cancer Res</u>. 2006 Aug 1;66(15):7661-7.</p> <p>[3]. Finn RS, et al. PD 0332991, a selective cyclin D kinase 4/6 inhibitor, preferentially inhibits proliferation of luminal estrogen receptor-positive human breast cancer cell lines in vitro. <u>Breast Cancer Res</u>. 2009;11(5):R77.</p>

源叶生物